

WHAT IS CLAIMED IS:

1. A method for preparing a nitric oxide-releasing substrate comprising: (a) contacting an amine-functionalized silane residue with a substrate; (b) contacting the amine-functionalized silane residue with a cross-linking agent; and (c) contacting at least one nitric oxide-releasing functional group with the cross-linked amine-functionalized silane residue.
2. The method according to claim 1, wherein the substrate comprises a metal, glass, plastic, rubber, or ceramic.
3. The method according to claim 2, wherein the substrate comprises a metal.
4. The method according to claim 3, wherein the metal is selected from the group consisting of gold or gold alloys, metal substrates having a gold-containing coatings, titanium and titanium alloys, metal substrates having a titanium-containing coatings, nickel or nickel alloys, metal substrates having a nickel-containing coatings, silicon and silicon alloys; metal substrates having a silicon-containing coatings, aluminum and aluminum alloys, metal substrates having an aluminum-containing coatings, zinc and zinc alloys, metal substrates having a zinc-containing coatings, magnesium alloys, tin and tin alloys, metal substrates having a tin-containing coating, copper and copper alloys, and metal substrates having a copper-containing coatings.
5. The method according to claim 3, wherein the metal is stainless steel.
6. The method according to claim 2, wherein the substrate comprises glass.
7. The method according to claim 6, wherein the glass is selected from the group consisting of soda lime glass, strontium glass, barium glass, borosilicate glass, and glass-ceramics comprising lanthanum.
8. The method according to claim 2, wherein the substrate comprises a plastic.

9. The method according to claim 8, wherein the plastic is selected from the group consisting of acrylics, acrylonitrile-butadiene-styrene, acetals, polyphenylene oxides, polyimides, polystyrene, polypropylene, polyethylene, polytetrafluoroethylene, polyvinylidene, polyethylenimine, polyesters, polyethers, polylactones, polyurethanes, polycarbonates, polyethylene terephthalate, and combinations thereof.

10. The method according to claim 2, wherein the substrate comprises rubber.

11. The method according to claim 10, wherein the rubber is selected from the group consisting of silicones, fluorosilicones, nitrile rubbers, silicone rubbers, fluorosilicone rubbers, polyisoprenes, sulfur-cured rubbers, isoprene-acrylonitrile rubbers, and combinations thereof.

12. The method according to claim 2, wherein the substrate comprises a ceramic.

13. The method according to claim 12, wherein the ceramic is selected from the group consisting of alumina, silicon nitride, boron carbide, boron nitride, silica, and combinations thereof.

14. The method according to claim 1, wherein the amine-functionalized silane is selected from the group consisting of 3-aminopropyltrimethoxysilane, 3-aminopropyltriethoxysilane, 3-aminopropyldimethoxysilane, N-(3-acryloxy-2-hydroxypropyl)-3-amino-propyltriethoxysilane, N-2-(aminoethyl)-3-aminopropyltris(2-ethyl-hexoxy)silane, 3-(m-aminophenoxy)propyltrimethoxysilane, 3-(1-aminopropoxy)-3,3-dimethyl-1-propenyl-trimethoxysilane, 3-aminopropyltris(methoxyethoxyethoxy)silane, 3-aminopropylmethyldiethoxysilane, 3-aminopropyltris(trimethylsiloxy)silane, bis(dimethylamino)methylchlorosilane, bis(dimethylamino)methylmethoxysilane, bis(dimethylamino)phenylchlorosilane, bis(dimethylamino)phenylethoxysilane, bis(2-hydroxyethyl)-3-aminopropyltriethoxysilane, bis(2-hydroxyethyl)-3-aminopropyltrimethoxysilane, bis(3-triethoxysilyl)propylamine, 1,4-bis[3-

(trimethoxysilyl)propyl]ethylenediamine, (N,N-diethyl-3-aminopropyl)trimethoxysilane, (N,N-dimethyl-3-aminopropyl)trimethoxysilane, N-phenylaminopropyltrimethoxysilane, trimethoxysilylpropyldiethylenetriamine, trimethoxysilylpropylpentaethylenehexamine, triethoxysilyloctyldiethylenetriamine, triisopropoxysilylpentaethylenehexamine, n-trimethoxysilylpropyl-N,N,N-trimethylammonium chloride, 3-aminopropylmethyldiethoxysilane, 2-(perfluorooctyl)ethyltriaminotrimethoxysilane, 4-aminobutyltrimethoxysilane, N-(6-aminoethyl)aminopropyltrimethoxysilane, 3-(dimethoxymethylsilylpropyl)diethylenetriamine, N-(2-aminoethyl)-N'-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine, amine-functionalized polydimethylsiloxane copolymer, and bis-aminosilane.

15. The method according to claim 1, wherein the cross-linking agent comprises a dihalogenated alkyl or a dihalogenated aryl.

16. The method according to claim 15, wherein the cross-linking agent is substituted with a substituent selected from the group consisting of an alkyl, a cycloalkyl, hydroxyl, nitro, a halogen, cyano, and combinations thereof.

17. The method according to claim 16, wherein the cross-linking agent is 1,4-dibromoethane or 1,5-difluoro-2,4-dinitrobenzene.

18. The method according to claim 1, wherein the nitric oxide-releasing functional group comprises a nitric oxide-releasing functional group that is an O²-protected diazeniumdiolate of an amine-functionalized silane.

19. The method according to claim 1, wherein the amine-functionalized silane residue is dissolved in a solvent comprising at least one molar equivalent of water.

20. A method for preparing a nitric oxide-releasing metallic substrate comprising: (a) contacting the aminopropyltrimethoxysilane solution with a substrate; (b) contacting the aminopropyltrimethoxysilane with a cross-linking agent selected from the

group consisting of 1,4-dibromoethane and 1,5-difluoro-2,4-dinitrobenzene; and (c) contacting an O²-protected diazeniumdiolate with the cross-linked aminopropyl-trimethoxysilane.

21. The method according to claim 20, wherein the amine-functionalized silane residue is dissolved in a solvent comprising at least one molar equivalent of water.

22. A method for preparing a nitric oxide-releasing substrate comprising: (a) contacting the amine-functionalized silane residue solution with a substrate; (b) contacting the amine-functionalized silane residue with a cross-linking agent; (c) contacting at least one nucleophilic residue with the cross-linked amine-functionalized silane residue; and (d) contacting the nucleophilic residue with nitric oxide gas.

23. The method according to claim 22, wherein the nucleophilic residue is an amine-derived residue.

24. The method according to claim 23, wherein the amine-derived residue is selected from the group consisting of diethylenetriamine, pentaethylenhexamine, high molecular weight linear/branched polyethylenimines, amine-functionalized divinylbenzene, piperazine, and combinations thereof.

25. The method according to claim 22, further comprising: after step (c), contacting the nucleophilic residue with a cross-linking agent, and contacting at least one additional nucleophilic residue with the cross-linked nucleophilic residue.

26. The method according to claim 22, further comprising: prior to step (d), treating the substrate having the cross-linked amine-functionalized silane residue with a biocompatible topcoat.

27. The method according to claim 26, wherein the biocompatible topcoat is a lubricious hydrogel.

28. The method according to claim 27, wherein the lubricious hydrogel is selected from the group consisting of homo- and heteropolyethers, polyols, polyureas, polylactones, albumin-, heparin-, and polyphosphorylcholine-functionalized polymers, and combinations thereof.

29. The method according to claim 22, wherein the amine-functionalized silane residue is dissolved in a solvent comprising at least one molar equivalent of water.

30. A method for preparing a nitric oxide-releasing substrate comprising: (a) contacting an aminopropyl-trimethoxysilane with a substrate; (b) contacting the aminopropyltrimethoxysilane with a cross-linking agent selected from the group consisting of 1,4-dibromoethane and 1,5-difluoro-2,4-dinitrobenzene; (c) contacting an amine-derived residue selected from the group consisting of diethylenetriamine, pentaethylenhexamine, high molecular weight linear/branched polyethylenimines, amine-functionalized divinylbenzene, and piperazine with the cross-linked aminopropyltrimethoxysilane; and (d) contacting the amine-derived residue with nitric oxide gas.

31. The method according to claim 30, wherein the amine-functionalized silane residue is dissolved in a solvent comprising at least one molar equivalent of water.

32. A medical device for delivering nitric oxide in a therapeutic concentration, the device comprising a substrate having nitric oxide bound thereto through a diazeniumdiolated nucleophile bonded to a silane intermediate, the silane intermediate being amine-functionalized and cross-linked.

33. The medical device according to claim 32, wherein the device comprises metal.

34. The medical device according to claim 33, wherein the metal is stainless steel.

35. The medical device according to claim 32, wherein the silane intermediate is selected from the group consisting of 3-aminopropyltrimethoxysilane, 3-aminopropyltriethoxysilane, 3-aminopropyldimethoxysilane, N-(3-acryloxy-2-hydroxypropyl)-3-amino-propyltriethoxysilane, N-2-(aminoethyl)-3-aminopropyltris(2-ethyl-hexoxy)silane, 3-(m-aminophenoxy)propyltrimethoxysilane, 3-(1-aminopropoxy)-3,3-dimethyl-1-propenyl-trimethoxysilane, 3-aminopropyltris(methoxyethoxyethoxy)silane, 3-aminopropylmethyldiethoxysilane, 3-aminopropyltris(trimethylsiloxy)silane, bis(dimethylamino)methylchlorosilane, bis(dimethylamino)methylmethoxysilane, bis(dimethylamino)phenylchlorosilane, bis(dimethylamino)phenylethoxysilane, bis(2-hydroxyethyl)-3-aminopropyltriethoxysilane, bis(2-hydroxyethyl)-3-aminopropyltrimethoxysilane, bis(3-triethoxysilyl)propylamine, 1,4-bis[3-(trimethoxysilyl)propyl]ethylenediamine, (N,N-diethyl-3-aminopropyl)trimethoxysilane, (N,N-dimethyl-3-aminopropyl)trimethoxysilane, N-phenylaminopropyltrimethoxysilane, trimethoxysilylpropyldiethylenetriamine, trimethoxysilylpropylpentaethylenehexamine, triethoxysilyloctyldiethylenetriamine, triisopropoxysilylpentaethylenehexamine, n-trimethoxysilylpropyl-N,N,N-trimethylammonium chloride, 3-aminopropylmethyldiethoxysilane, 2-(perfluorooctyl)ethyltriaminotrimethoxysilane, 4-aminobutyltrimethoxysilane, N-(6-aminohexyl)aminopropyltrimethoxysilane, 3-(dimethoxymethylsilylpropyl)diethylenetriamine, N-(2-aminoethyl)-N'-[3-(dimethoxymethylsilyl)propyl]-1,2-ethanediamine, amine-functionalized polydimethylsiloxane copolymer, and bis-aminosilane.

36. The medical device according to claim 32, wherein the silane intermediate is cross-linked using a cross-linking agent.

37. The medical device according to claim 36, wherein the cross-linking agent is a dihalogenated alkyl or a dihalogenated aryl.

38. The medical device according to claim 37, wherein the cross-linking agent is substituted with a substituent selected from the group consisting of an alkyl, a cycloalkyl, hydroxyl, nitro, a halogen, and cyano.

39. The medical device according to claim 38, wherein the cross-linking agent is 1,4-dibromoethane or 1,5-difluoro-2,4-dinitrobenzene.

40. The medical device according to claim 32, wherein the diazeniumdiolated nucleophile comprises a nitric oxide-releasing functional group that is an O²-protected diazeniumdiolate of an amine-functionalized silane.

41. The medical device according to claim 32, wherein the medical device is selected from the group consisting of an arterial stent, guide wire, catheter, trocar needle, bone anchor, bone screw, protective plating, hip and joint implant, electrical lead, biosensor, and a probe.

42. An arterial stent for delivering nitric oxide in a therapeutic concentration, the device comprising a metallic substrate having nitric oxide releasably bound thereto through an O²-protected diazeniumdiolate bonded to an aminopropyltrimethoxysilane, the aminopropyltrimethoxysilane being cross-linked by a cross-linking agent selected from the group consisting of 1,4-dibromoethane and 1,5-difluoro-2,4-dinitrobenzene.

43. A method for preparing a nitric oxide-releasing substrate comprising: (a) contacting a non- or weakly-nucleophilic silane residue with a substrate; (b) contacting the silane residue with a cross-linking agent; and (c) contacting nitric oxide with the cross-linked silane residue.